UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and ASTRAZENECA AB, Plaintiffs/Counterclaim-Defendants, v. SANDOZ INC., Defendant/Counterclaim-Plaintiff.	Civil Action No. 14-cv-03547-RMB-KMW **SANDOZ INC. AND SAGENT PHARMACEUTICALS, INC.'S JOINT OPENING CLAIM CONSTRUCTION BRIEF**
ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, and ASTRAZENECA AB, Plaintiffs/Counterclaim-Defendants, v. SAGENT PHARMACEUTICALS, INC., Defendant/Counterclaim-Plaintiff.	Civil Action No. 14-cv-05539-RMB-KMW

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I. Introduction

The four Patents-in-Suit (U.S. Pat. Nos. 6,774,122 ("the '122 patent") (Ex. A); 7,456,160 ("the '160 patent") (Ex. B); 8,329,680 ("the '680 patent") (Ex. C); 8,466,139 ("the '139 patent") (Ex. D) (collectively, the "Patents-in-Suit")[1] in this Abbreviated New Drug Application ("ANDA") litigation relate to injectable formulations of an anti-estrogen compound colloquially known as both "fulvestrant" and "ICI 182,780." AstraZeneca AB is listed as the assignee of each of the Patents-in-Suit.

Sandoz Inc. ("Sandoz") and Sagent Pharmaceuticals, Inc. ("Sagent") (collectively, "Defendants") have asserted that the Patents-in-Suit are not infringed and that each is invalid for anticipation, obviousness, lack of enablement, lack of written description, and indefiniteness. Several claim construction-related issues below bear on those defenses. Consequently, Plaintiffs have approached claim construction with a view toward narrowing the claims; such narrowing is not, however, based on intrinsic evidence. As discussed in more detail below, each of Plaintiffs' attempts is improper because the claim language is broad, and the specification contains many (non-limiting) embodiments. Moreover, there was no disavowal of scope of any claim, and the one time that Plaintiffs used special lexicography, it was to *broaden* the term "fulvestrant." (*See infra* at 6-8).

In contrast to Plaintiffs' constructions, Defendants' constructions rely on the intrinsic evidence, and clearly state how the terms would be read and understood by an ordinarily skilled artisan in view of that intrinsic evidence. Thus, Defendants' constructions should be adopted,

[1] All exhibits are attached to the Declaration of Debra A. Lange, dated May 7, 2015, submitted concurrently herewith.

and Plaintiffs' erroneous constructions should be rejected.[2]

II. Factual Background

The reference listed drug in this ANDA litigation is Faslodex®, which is indicated "for the treatment of hormone receptor positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy." Ex. F, Faslodex® Package Insert. There are no other FDA-approved Faslodex® indications.[3] The Patents-in-Suit do not involve a new compound. By the relevant time frame, fulvestrant was a known anti-estrogen compound, and there had long been "interest in the development of the drug as a therapeutic agent for oestrogen-dependent indications such as breast cancer and certain benign gynaecological conditions." Ex. A, '122 pat., col. 1, ll. 59-62; *see also id*. at Cover (U.S. Patents; Foreign Patents; Other Publications)[4]. The Patents-in-Suit purport to cover a particular method of dosing fulvestrant formulations.

According to the Patents-in-Suit, "[f]ulvestrant shows, along with other steroidal based compounds, certain physical properties which make formulation of these compounds difficult. Fulvestrant is a particularly lipophilic molecule . . . and its aqueous solubility is extremely low at around 10 ng/ml . . . ." Ex. A, '122 pat., col. 2, ll. 46-51. The Patents-in-Suit purport to solve this solubility problem by providing a "novel sustained release pharmaceutical formulation adapted for administration by injection." *Id.* at Abstract. The claimed formulations are

[2] Attached as Exhibit E is a list from the March 23, 2015 Joint Claim Construction and Prehearing Statement reflecting claim constructions on which the parties agree.

[3] [redacted]

[4] The Patents-in-Suit in suit are related and share a specification. For brevity and convenience, citations to the patents herein are to the '122 patent, unless otherwise specified.

comprised of "fulvestrant,"[5] "ethanol,"[6] benzyl benzoate, benzyl alcohol, and a "sufficient amount of castor oil."[7] *See generally* Exs. A-D, Patents-in-Suit. Every claim requires that each excipient be present in a certain amount, most often "about 10% ethanol," "about 10% benzyl alcohol," and "about 15% benzyl benzoate"—*e.g.*, an ~10-10-15 ratio. *See id.*

The Patents-in-Suit's applicants attempted to achieve patentability for their allegedly-novel formulation by distinguishing prior art. For example, during the '122 patent prosecution, the applicants added the required percentages of each excipient to narrow the claims to distinguish "Dukes." Ex. H, '122 pat. PH, 12/29/2003 Amendment. During the subsequent '680 patent prosecution, the applicants distinguished "McLeskey," which expressly *disclosed a fulvestrant formulation in castor oil having the same 10% ethanol-10% benzyl alcohol-15% benzyl benzoate (10-10-15) ratio as those claimed in the Patents-in-Suit*. *See* Ex. I, '680 pat. PH, 1/17/2012 Sawchuk § 132 Decl. (exhibits omitted).

To get around McLeskey—and despite the fact that McLeskey used "preformulated ICI 182,780" supplied by "Zeneca Pharmaceuticals" (Ex. J, McLeskey at 698, 709)—applicants averred that McLeskey's formulation was not *actually* identical to the claims AstraZeneca AB sought. In a tortuous twenty-six-page § 132 declaration having seventeen exhibits, the applicants averred via Dr. Ronald Sawchuk that, *inter alia*:

(i) McLeskey had not specified whether the formulation's ratios were weight-to-weight or weight-to-volume;

(ii) the exact nature of the excipients (including "ethanol") was crucial to understanding the real make-up of McLeskey's formulation; and

(iii) after doing various calculations, Dr. Sawchuk concluded that despite the fact that McLeskey *reported* a 10-10-15 ratio of excipients using Zeneca's pre-formulated ICI

[5] This term is before the court for construction.
[6] This term is before the court for construction.
[7] This term is before the court for construction.

182,780, McLeskey did not actually *have* a 10-10-15 ratio of excipients.

See Ex. I, '680 pat. PH, 1/17/2012 Sawchuk § 132 Decl., ¶ 16 ("McLeskey does not specify whether the percentages in the castor oil composition are in weight/volume units (% w/v, as recited in the claims of the '887 application) or in volume/volume units (% v/v)."); *id.* at 9 n.1 ("McLeskey does not indicate whether the ethanol used in its castor oil fulvestrant composition is dehydrated ethanol or the binary azeotropic ethanol composition containing about 96% ethanol by volume."); *id.* at ¶¶ 23-30 (calculations).

While the applicants made narrowing amendments regarding the exact make-up of the *formulation*, each Patent-in-Suit issued with two expansive independent claims to "a method of treating a hormonal dependent benign or malignant disease of the breast or reproductive tract" by administration (to a human in need of such treatment) an intra-muscular injection of a specific formulation of "fulvestrant" (which the applicants broadened further by defining fulvestrant as including "pharmaceutically-acceptable salts thereof and any possible solvates thereof"). Ex. A, '122 pat., col. 1, l. 64 - col. 2, l. 2; *see also* Exs. A-D, Claims.

III. Applicable Legal Principles

The ultimate interpretation of a patent claim is a legal conclusion and a judge's resolution of an underlying factual dispute can only be overturned upon a showing of clear error. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 841 (2015). To construe a claim, a "court looks first to the intrinsic evidence of record, examining, in order, the claim language itself, the specification, and the prosecution history." *Alza Corp. v. Mylan Labs., Inc.*, 391 F.3d 1365, 1370 (Fed. Cir. 2004). Claims must "inform those skilled in the art about the scope of the invention

with reasonable certainty," when read in light of the specification and prosecution history.[8] *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2129 (2014). Claim terms are generally given their plain and ordinary meanings to one of skill in the art when read in the context of the specification and prosecution history. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc).

"There are only two exceptions to this general rule: 1) when a patentee sets out a definition and acts as his own lexicographer, or 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012); *see also Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014) (depart from the plain and ordinary meaning based on the specification in only two instances: lexicography and disavowal).

As to lexicography, "the specification 'acts as a dictionary when it expressly defines terms used in the claims . . . .'" *Phillips*, 415 F.3d at 1321. And "[u]nder the lexicographer rule, an inventor acts as an independent lexicographer and can even give claim terms a meaning 'inconsistent with its ordinary meaning.'" *Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1378 (Fed. Cir. 2005) (quoting *Boehringer Ingelheim Vetmedica, Inc. v. Schering–Plough Corp.*, 320 F.3d 1339, 1347 (Fed. Cir. 2003)); *see also, e.g.*, *Phillips*, 415 F.3d at 1316 ("[O]ur cases recognize that the specification may reveal a special definition given to a claim term by the

[8] The development of pharmaceutically effective formulations is multi-disciplinary, and can involve collaborative work of professionals in many disciplines, including biology, medicine, chemistry, medicinal chemistry, organic synthesis, pharmacology, formulation, and drug delivery, among others. Individuals who work in these disciplines typically have an advanced degree (*e.g.*, Pharm. D., M.D., or Ph.D.) in a relevant field, as well as several years of research experience. The person of ordinary skill in the art to which the Patents-in-Suit pertain would understand that the process of developing pharmaceutically effective formulations requires a multi-disciplinary approach, and would take advantage of the specialized skills of others.

patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs."); *Int'l Rectifier Corp. v. IXYS Corp.*, 361 F.3d 1363, 1373 (Fed. Cir. 2004) (patentee defining "annular," which usually means in the shape of a ring, to describe structures that are not circular or curved, but polygonal).

As to disavowal, the Federal Circuit has recently confirmed the standards are "exacting." *Southco, Inc. v. Fivetech Tech. Inc*., No. 2014-1390, 2015 WL 1609846, at *6 (Fed. Cir. Apr. 10, 2015). For example, the Federal Circuit has held that disavowal applies when the patentee makes statements such as "the present invention requires" or "the present invention is" or "all embodiments of the present invention are. . . ." *See Regents of Univ. of Minn. v. AGA Med. Corp*., 717 F.3d 929, 936 (Fed. Cir. 2013); *Honeywell Int'l, Inc. v. ITT Indus., Inc.*, 452 F.3d 1312, 1317-20 (Fed. Cir. 2006); *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1343-44 (Fed. Cir. 2001); *AstraZeneca AB v. Hanmi USA, Inc.*, 554 F. App'x 912, 915 (Fed. Cir. 2013). The Federal Circuit has also found disclaimer when the patent repeatedly disparages an embodiment. *See Chi. Bd. Options Exch., Inc. v. Int'l Sec. Exch., LLC*, 677 F.3d 1361, 1372 (Fed. Cir. 2012)*; Hill-Rom Servs.*, 755 F.3d at 1372-73, 1377 (finding no disclaimer or lexicography where the specification did not: (i) contain "words of manifest exclusion or restriction"; (ii) require the invention to have the feature at issue; (iii) extoll the virtues of the feature; (iv) disparage technology without the feature; nor (v) state that the feature was an "important, essential, or critical part" of the invention).

Lastly, while claims are read "in view of the specification," courts "do not read limitations from the embodiments in the specification into the claims." *Hill-Rom Servs., 755* F.3d at 1371 (citing *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 904 (Fed. Cir. 2004)). This is especially true when the purported limitation is "based upon a term not appearing in the

claim." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1325 (Fed. Cir. 2003).

IV. Disputed Claim Terms

A. "Fulvestrant"

The term "fulvestrant" is present in every independent claim of the Patents-in-Suit (and thus is also present in every dependent claim of the Patents-in-Suit).

Term	Defendants' Construction[9]	Plaintiffs' Construction
"fulvestrant"	"7α-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17β-diol, including pharmaceutically acceptable salts thereof, and any possible solvates of either thereof"	Plain and ordinary meaning to a person of skill in the art—i.e., the international non-proprietary name for the chemical compound, 7α-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17β-diol.

While the constructions proffered by Plaintiffs and Defendants for the term "fulvestrant" include the same chemical name ("7α . . . diol"), they fundamentally differ in that Plaintiffs would stop at the chemical name, while Defendants include the pharmaceutically acceptable salts, and any possible solvates of either thereof. Defendants include this additional text because the patentees clearly and expressly chose to be their own lexicographers with regard to this term.

As noted, the plain and ordinary meaning of a term is the proper construction ***except*** in two circumstances: lexicography and disavowal. *Thorner*, 669 F.3d at 1365; *Hill-Rom Servs.*, 755 F.3d at 1371. Here, because the patentees clearly and expressly availed themselves of special lexicography for the term "fulvestrant," Plaintiffs' restriction of the term to the "plain and ordinary" chemical structure linked with the non-proprietary name is overly-limiting.

The specification expressly defines fulvestrant in a two-sentence passage, with the second sentence containing the special lexicography:

[9] To the extent there are any differences between Sandoz's and Sagent's proposed constructions, Sagent adopts the constructions proposed by Sandoz.

> 7α-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17β-diol, or ICI 182,780, has been allocated the international non-proprietary name fulvestrant, which is used hereinafter. ***When referring to fulvestrant we include pharmaceutically-acceptable salts thereof and any possible solvates of either thereof***.

Ex. A, '122 pat., col. 1, l. 64-col. 2, l. 2 (emphasis added). Given the applicants' clear, express, and unequivocal statement that the term "fulvestrant" "include[s] pharmaceutically-acceptable salts thereof and any possible solvates of either thereof," the specification here "acts as a dictionary" and "expressly defines terms used in the claims. . . ." *Phillips*, 415 F.3d at 1321; *see also, e.g., ViiV Healthcare UK Ltd. v. Lupin Ltd.*, 904 F. Supp. 2d 379, 381(D. Del. Nov. 16, 2012) (construing "physiologically functional derivative" exactly as set forth in the specification of U.S. Patent No. 6,417,191, where the specification states: "As used herein, the term 'physiologically functional derivative' includes . . . .") and Ex. U, Patent No. 6,417,191, col. 2, ll. 32-33. Here, the specification expressly broadens the term "fulvestrant" beyond merely the non-proprietary name / structure to include salts and solvates thereof.

Therefore, Defendants' construction—which mirrors the controlling two-sentence passage from the specification—can be the only legally correct construction. *Compare* Ex. A, '122 pat., col. 1, l. 64 - col. 2, l. 2 *with* Defendants' Construction. It follows that any arguments Plaintiffs make in support of their "plain and ordinary meaning" construction are inapposite and legally wrong. *See Hill-Rom Servs.*, 755 F.3d at 1371.

Thus, Defendants respectfully submit that their construction—"7α-[9-(4,4,5,5,5-pentafluoropentylsulphinyl)nonyl]oestra-1,3,5(10)-triene-3,17β-diol, including pharmaceutically acceptable salts thereof, and any possible solvates of either thereof"—is correct; gives full meaning to the term consistent with the specification; and that the Court should adopt Defendants' construction for the term "fulvestrant."

B. "Administration/administering to a human in need of such treatment"

The language "administration/administering to a human in need of such treatment" appears in every independent claim of the Patents-in-Suit (and is thus also present in every dependent claim of the Patents-in-Suit).

Term	Defendants' Construction	Plaintiffs' Construction
"administration to a human in need of such treatment"	Plain and ordinary meaning – i.e., administration to a human having a hormonal dependent benign or malignant disease of the breast or reproductive tract.	Plain and ordinary meaning to a person of skill in the art—i.e., administration to a human with a disease (as limited by the claims) that could benefit from the method of treating.

Defendants' and Plaintiffs' proposed constructions agree that a plain and ordinary meaning applies to "administration to a human in need of such treatment," but differ as to what qualifies as "such treatment," which impacts invalidity issues. *See Gen. Elec. Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 370-71, 375 (1938) (validity analysis considered whether phrase "of such size and contour" adequately differentiated prior art filaments).

Defendants' construction is based on the structure and language of the claims, the specification, and common sense. Plaintiffs' construction is ambiguous, and does not comport with the purpose of claim construction. Plaintiffs' construction also leaves room to: (i) improperly import limitations from the specification into the claims to avoid Defendants' § 112 defenses; and (ii) violate the doctrine of claim differentiation. Thus, the Court should reject Plaintiffs' construction and adopt Defendants' construction.

1. Defendants' construction is consistent with the claims themselves.

"[A] claim construction analysis must begin and remain centered on the claim language itself, for that is the language the patentee has chosen to 'particularly point[ ] out and distinctly claim[ ] the subject matter which the patentee regards as his invention.'" *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004).

Defendants' construction properly comports with the language and structure of the claims. Here, two different clauses of each independent claim are linked by terms having the same root word, "treat," *e.g.*:

> A method of ***treating*** a hormonal dependent benign or malignant disease of the breast or reproductive tract by administration to a human in need of ***such treatment*** an intra-muscular injection of a pharmaceutical formulation comprising . . . .

Ex. A, '122 pat., claim 1 (emphasis added).

> A method for ***treating*** a hormonal dependent benign or malignant disease of the breast or reproductive tract comprising administering intramuscularly to a human in need of ***such treatment*** a formulation comprising . . . .

Ex. D, '139 pat., claim 1 (emphasis added).

Defendants' proposed construction states that "such treatment" corresponds to the one the claims expressly provide: "a hormonal dependent benign or malignant disease of the breast or reproductive tract." Ex. A, '122 pat., claim 1. Plaintiffs seek to rewrite the above-underlined text to mean, "a disease (as limited by the claims) that could benefit from the method of treating." That is circular, does not clarify claim scope, and if anything, creates ambiguity.

Other courts have construed the term "human in need of such treatment" exactly as Defendants advocate. In *Pfizer Inc. v. Teva Pharmaceuticals. USA, Inc.*, the district court construed the term "a male human [animal] in need of such treatment." 803 F. Supp. 2d 397, 408 (E.D. Va. 2011). The claim at issue read, in relevant part: "[a] method of ***treating*** erectile dysfunction in a male human, comprising orally administering to a male human in need of such ***treatment*** an effective amount of a compound selected from. . . ." *Id.* at 404 (emphasis added). The court found that "'such treatment' in this term referred back to 'treating erectile dysfunction.'" *Id.* at 408. The court then stated "the meaning of the term is clear" and adopted the construction "a male human in need of treatment for erectile dysfunction." *Id.*

Applying *Pfizer*, the plain language and structure of the claims shows that "administration to a human in need of such treatment" refers back to the "method of treating a hormonal dependent benign or malignant disease of the breast or reproductive tract." The "human in need of such treatment" is a human having a "hormonal dependent benign or malignant disease of the breast or reproductive tract." This is exactly what Defendants' construction says.

2. Defendants' construction is fully supported by the specification.

The specification also supports the claims' plain language—and thus, Defendants' construction. *See* Ex. A, '122 pat., col. 1, ll. 17-19 ("Oestrogen deprivation is fundamental to the treatment of many benign and malignant diseases of the breast and reproductive tract."); *id.*, col. 11, ll. 4-8 ("A further feature of the invention is a method of treating a benign or malignant diseases of the breast or reproductive tract, preferably treating breast cancer, by administration to a human in need of such treatment by intra-muscular injection an extended release ricinoleate vehicle …."); *id.*, col. 11, ll. 18-22 ("A further feature of the invention is use of fulvestrant in the preparation of a pharmaceutical formulation as describe hereinabove, for the treatment of a benign or malignant disease of the breast or reproductive tract, preferably treating breast cancer."); *id.*, col. 11, ll. 27-29 ("As described above fulvestrant is useful in the treatment of oestrogen-dependent indications such as breast cancer and gynaecological conditions, such as endometriosis."). Thus, there was no lexicography or disavowal, and the term should be given its plain and ordinary meaning. *Thorner*, 669 F.3d at 1365*; Hill-Rov Servs.*, 755 F.3d at 1371.

In short, there is no support for Plaintiffs' construction anywhere in the Patents-in-Suit.

3. Plaintiffs' construction should be rejected because it is ambiguous.

Plaintiffs' construction raises more questions than it answers—*e.g.*, who exactly "could benefit" from the method of treating; how is that determination made; who makes it; and when?

The Federal Circuit has explained (discussed *infra* at 21-22) that construing a claim based on terms not appearing in the claims (here, "could benefit") is quite dangerous. *See Amgen*, 314 F.3d at 1325 ("The danger of improperly importing a limitation is even greater when the purported limitation is based upon a term not appearing in the claim. 'If we once begin to include elements not mentioned in the claim in order to limit such claim . . . , we should never know where to stop.'"); *Source Vagabond Sys. Ltd. v. Hydrapak, Inc.*, 753 F.3d 1291, 1299-300 (Fed. Cir. 2014) (approving the district court's statement that: "an 'analysis' that adds words to the claim language [without support in the intrinsic evidence]" does not follow "'standard canons of claim construction.'").

4. Plaintiffs' construction improperly rewrites claim language.

Why Plaintiffs want to change the scope of "such treatment" to any diseases "that could benefit from the method of treating" is obvious—it gives them the flexibility to cover any disease where the drug works (for infringement purposes), while excluding any disease where the drug does not work (for invalidity purposes), at whatever time is convenient to Plaintiffs. Claims are not a "nose of wax" shifting in scope whether the art advances or retrenches. Plaintiffs chose the scope of diseases they sought to claim; whether that may constitute over- or under-claiming a decade later is of no moment; the words of the claim should be given effect.

a. It is improper to limit claims to one embodiment.

The Faslodex® commercial product achieved an indication for only one disease in one population (post-menopausal women); the claims are not so limited, and "[i]t is the claims that measure the invention." *SRI Int'l v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985) (en banc). Thus, to the extent that Plaintiffs are attempting to limit the claims to anything other than treatment of "***many*** benign and malignant diseases of the breast and reproductive tract" (Ex. A, '122 Pat., col. 1, ll. 17-19 (emphasis added)), Plaintiffs' construction is improper.

It is axiomatic that courts "do not read limitations from the embodiments in the specification into the claims." *Hill-Rom Servs.*, 755 F.3d at 1371; *see also, e.g.*, *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1287 (Fed. Cir. 2010) ("It is therefore important not to confuse exemplars or preferred embodiments in the specification that serve to teach and enable the invention with limitations that define the outer boundaries of claim scope.").

Nor did the patentees disavow any portion of treatment of "a hormonal dependent benign or malignant disease of the breast or reproductive tract" in a way that comports with Plaintiffs' proposed construction. Ex. A, '122 pat., col. 1, ll. 17-19; *id.*, col. 11, ll. 4-8, 18-22, 27-29; *see also Hill-Rom Servs.*, 755 F.3d at 1371 ("exacting" standard for disavowal); *Liebel-Flarsheim*, 358 F.3d at 906 ("Even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using 'words or expressions of manifest exclusion or restriction.'"); *Hoganas AB v. Dresser Indus., Inc.*, 9 F.3d 948, 950 (Fed. Cir. 1993) ("It is improper for a court to add 'extraneous' limitations to a claim, that is, limitations added 'wholly apart from any need to interpret what the patentee meant by particular words or phrases in the claim.'").

If anything, the specification confirms claim breadth, given its repeated references to diseases—***plural***—of the breast ***and*** reproductive tract. Ex. A, '122 pat., col. 1, ll. 17-19; *id.*, col. 11, ll. 4-8, 18-22, 27-29.

Thus, Plaintiffs' construction fails for the discrete reason that its ambiguity allows for improper importation of limitations from the specification into the claims.

b. The doctrine of claim differentiation should be applied.

Furthermore, if Plaintiffs' construction does not include "many benign and malignant diseases of the breast and reproductive tract" (Ex. A, '122 pat., col. 1, ll. 17-19), then it does not comport with the doctrine of claim differentiation. Indeed, if the independent claims were

limited to, for example, only breast cancer, then there would be no need for dependent claims drawn to breast cancer. Dependent claims cannot be broader than the claim from which they depend. *Alcon Research, Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1367 (Fed. Cir. 2012) (citing 35 U.S.C. § 112, ¶ 4); *Intamin Ltd. v. Magnetar Techs., Corp.*, 483 F.3d 1328, 1335 (Fed. Cir. 2007) ("An independent claim impliedly embraces more subject matter than its narrower dependent claim."); *Liebel-Flarsheim,* 358 F.3d at 910 ("[T]he presence of a dependent claim that adds a particular limitation raises a presumption that the limitation in question is not found in the independent claim."); *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1242 (Fed. Cir. 2003) ("[D]ependent claims are presumed to be of narrower scope than the independent claims from which they depend."). Thus, the independent claims should be construed broadly, and in accordance with the plain meaning of "benign and malignant diseases of the breast and reproductive tract."[10] Thus, Defendants respectfully request that the Court adopt their proposed construction for "administration to a human in need of such treatment."

C. "Sufficient amount of a castor oil vehicle"

The term "sufficient amount of a castor oil vehicle" is present in every independent claim of the Patents-in-Suit (and is thus also present in every dependent claim of the Patents-in-Suit).

Term	Defendants' Construction	Plaintiffs' Construction
"sufficient amount of a castor oil vehicle"	There are multiple concepts that can be associated with the plain and ordinary meaning(s), including but not limited to: • sufficient amount of a castor oil to solubilize the active ingredient; • sufficient amount of a castor oil to bring the composition to a certain volume;	"after fulvestrant and the excipients, the remaining volume is filled with pharmaceutically-

[10] The extrinsic evidence also supports a broad construction, as the plain meaning of the terms "benign" and "malignant" are not restricted to particular diseases. *See, e.g.*, Exs. K, L, M (defining "benign" and "malignant"). Similarly, the extrinsic evidence confirms the broad scope of "reproductive tract," which is not gender-specific. *See, e.g.*, Exs. K, M, N.

	• sufficient amount of a castor oil to bring the composition to a certain weight; • sufficient amount of a castor oil needed to minimize precipitation of the injected formulation; • sufficient amount of a castor oil needed to render the injected formulation functional; • sufficient amount of a castor oil containing a particular proportion of triglycerides of ricinoleic acid; • sufficient amount of a particular grade of castor oil; • sufficient amount of a castor oil that conforms to a particular standard; • sufficient amount of a castor oil blended with other oils. The above list is not meant to be comprehensive.[11]	acceptable castor oil"

The construction proposed by Defendants for the term "sufficient amount of castor oil" differs markedly from Plaintiffs' construction in that Defendants' construction properly accounts for the lack of specificity in the claims, as well as the various embodiments disclosed in the specification.[12] In contrast—and in an attempt to try to give the illusion of definiteness—Plaintiffs' construction improperly limits the term to only one of the many disclosed embodiments. Thus, Defendants' construction should be adopted, and Plaintiffs' construction should be rejected.

[11] Defendants state that the presence of multiple plain and ordinary meanings of a claim term does not mean any one of these meanings is the correct construction of the term, and does not indicate any admission or acknowledgment by Defendants that the claim term has a meaning that satisfies the requirement of 35 U.S.C. § 112, ¶ 2. Additionally, Defendants reserve all rights to pursue various invalidity theories, including but not limited to indefiniteness theories under 35 U.S.C. § 112 for at least the reason that a person of ordinary skill in the art could read the term in various ways, as outlined above, and the appropriate scope of the claim language would change as a consequence. The specification does not provide necessary guidance as to the appropriate scope and meaning to apply to this term, nor does the prosecution history or other intrinsic evidence. The test for indefiniteness is still being developed and applied by the Federal Circuit following the U.S. Supreme Court's ruling in *Nautilus,* 134 S. Ct. 2120. Defendants specifically reserve all rights to make additional, modified, or different arguments regarding the same as Federal Circuit case law develops.

[12] Defendants' construction is further supported by extrinsic evidence. *See* Exs. K, L, M, O (defining the term "vehicle").

First, as a threshold issue, the claims provide no guidance as to the meaning of this term. Moreover, there are many embodiments disclosed in the specification; thus, every part of Defendants' construction corresponds to a different disclosed embodiment:

	Specification's Various Disclosures regarding a Sufficient Amount of a Castor Oil	**Relevant Part of Defendants' Construction**
1.	Table 4 (1st part) contains "**[s]olubility** comparisons of fulvestrant in oil based formulations…" Ex. A, '122 pat., col. 9, tbl. 4 (emphasis added).	to solubilize the active ingredient
2.	Table 3 reports all ingredients (including castor oil) as **weight-to-volume.** *Id.*, cols. 9-10; tbl. 3; *see also id.*, col. 2, ll. 65-66 (referring to volume); *id.*, col. 3, ll. 61-63 (need "sufficient castor oil to bring the solution to a volume of 1 ml").	to bring the composition to a certain volume
3.	Column 12 contains a "Flow Diagram of Manufacturing," which says "**Castor Oil → STAGE 3: MAKE TO WEIGHT.**" *Id.*, col. 12, ll. 15-35; *see also id.* at col. 11, l. 57 ("…the solution is made to final **weight** with castor oil …")	to bring the composition to a certain weight
4.	Table 4 (2nd part) reports the "[e]ffect of formulation on **precipitation** of fulvestrant at the injection site"; Figure 1 also reports the degree of **precipitation** at injection site. *Id.*, col. 10 & tbl. 4 (emphasis added).	to minimize precipitation of the injected formulation
5.	Column 6 specifically states that one needs a "sufficient amount of a ricinoleate vehicle so as to prepare a formulation **which is capable after injection of attaining a therapeutically significant blood plasma fulvestrant concentration** for at least 2 weeks. *Id.*, col. 6, ll. 12-15 (emphasis added).	to render the injected formulation functional
6.	"By the use of the term ricinoleate vehicle we mean an oil **which has as a proportion (at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 95% w/v) of its composition as triglycerides of ricinoleic acid**." *Id.*, col. 8, ll. 23-26 (emphasis added).	containing a particular proportion of triglycerides of ricinoleic acid
7.	"The ricinoleate vehicle may be a **synthetic oil or conveniently is castor oil**, ideally of pharmacopoeial standards, as described above." *Id.*, col. 8, ll. 26-28 (emphasis added).	sufficient amount of a particular grade of castor oil
8.	"The ricinoleate vehicle may be a synthetic oil or conveniently is castor oil, **ideally of pharmacopoeial standards**, as described above." *Id.*, col. 8, ll. 26-28 (emphasis added).	sufficient amount of a castor oil that conforms to a particular standard
9.	"By the use of the term ricinoleate vehicle we mean **an oil which has as a proportion** (at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 95% w/v) of its composition as	sufficient amount of a castor oil blended with other oils

	triglycerides of ricinoleic acid." *Id.*, col. 8, ll. 23-26 (emphasis added).	

In contrast, Plaintiffs' construction is limited to **one** embodiment only: the brought-to-volume disclosure. *Cf.* Defs.' Construction Embodiment No. 2, above. Thus, Plaintiffs' construction commits "one of the cardinal sins of patent law" by "reading a limitation from the written description into the claims." *Phillips*, 415 F.3d at 1320. The Federal Circuit "has expressly rejected the contention that [even] if a patent describes only a ***single*** embodiment, the claims of the patent must be construed as being limited to that embodiment." *Liebel–Flarsheim*, 358 F.3d at 906 (listing cases[13] rejecting attempts to import limitations from the specification into the claims) (emphasis added). The transgression is particularly egregious here because so many embodiments are expressly disclosed.

Second, the specification contains no "words of manifest exclusion or restriction," and does not require that the formulation be "brought to volume" with castor oil. Neither the specification nor the prosecution history contain evidence of disavowal—*a fortiori,* Plaintiffs cannot meet the "exacting" standard for same. *Hill-Rom Servs.*, 755 F.3d at 1371; *see also Liebel-Flarsheim*, 358 F.3d at 906 ("Even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using 'words or expressions of manifest exclusion or restriction.'").

[13] In *Liebel-Flarsheim*, the Federal Circuit cited and/or discussed: *ACTV, Inc. v. Walt Disney Co.*, 346 F.3d 1082, 1091 (Fed. Cir. 2003); *Apex Inc. v. Raritan Computer, Inc.*, 325 F.3d 1364, 1377 (Fed. Cir. 2003); *Altiris, Inc. v. Symantec Corp.*, 318 F.3d 1363, 1373 (Fed. Cir. 2003); *Tex. Digital Sys., Inc. v. Telegenix, Inc.*, 308 F.3d 1193, 1204-05 (Fed. Cir. 2002); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1327 (Fed. Cir. 2002); *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121 n. 14 (Fed. Cir. 1985) (en banc); *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1301 (Fed. Cir. 2003); *Altiris, Inc. v. Symantec Corp.*, 318 F.3d 1363, 1371 (Fed. Cir. 2003). *Liebel-Flarsheim*, 358 F.3d at 906.

Thus, it would be improper to narrow the scope of the term as Plaintiffs propose. Accordingly, Defendants respectfully ask the Court to adopt their proposed construction for the "sufficient amount of a castor oil vehicle" term.

D. "Whereby a therapeutically significant blood plasma fulvestrant concentration . . . is attained / achieved . . . ."

Various claims of the Patents-in-Suit require that a specified blood plasma concentration be either "achieved" or "attained" for a specified period of time. For convenience and brevity, Defendants present all of these "blood plasma terms" together, focusing on the core issue in dispute: the meaning of "attained . . . for" and/or "achieved . . . for."

Term	Defendants' Construction	Plaintiffs' Construction
whereby a therapeutically significant blood plasma fulvestrant concentration . . . is attained / achieved . . . for	There are multiple concepts that can be associated with the plain and ordinary meaning(s), including but not limited to: • whereby a therapeutically effective blood plasma concentration of at least 2.5 $ngml^{-1}$ is achieved by the patient in question at any point within two weeks after injection; • whereby a therapeutically effective blood plasma concentration of at least 2.5 $ngml^{-1}$ is achieved by the patient in question at any number of points within two weeks after injection; • whereby a therapeutically effective blood plasma concentration of at least 2.5 $ngml^{-1}$ is maintained by the patient in question for the entirety of two weeks after injection; • whereby a therapeutically effective blood plasma concentration of an average of at least 2.5 $ngml^{-1}$ is observed by the patient in question for the entirety of two weeks after injection; • whereby the mean therapeutically effective blood plasma concentration of a patient population is an average of at least 2.5 $ngml^{-1}$ for the entirety of two weeks after injection; • whereby the mean therapeutically effective blood plasma concentration of a patient population is at least 2.5 $ngml^{-1}$ for the entirety of two weeks after injection.	"the blood plasma fulvestrant concentration … is achieved and maintained…"

	The above list is not meant to be comprehensive.[14]	

Like the constructions for "sufficient amount of castor oil vehicle," the constructions proffered by Defendants for the term "whereby a therapeutically significant blood plasma fulvestrant concentration . . . is attained/achieved . . . for" differ from Plaintiffs' construction in that Defendants' construction properly accounts for the various potential plain and ordinary meanings of the phrase, while Plaintiffs improperly limit the term to only one embodiment in an attempt to preserve the claims' validity. Plaintiffs further err by adding ambiguous words to the construction that are not present anywhere in the Patents-in-Suit. Thus, Defendants' construction should be adopted, and Plaintiffs' construction should be rejected.

1. The claims do not use a term of art, and the specification does not provide the skilled artisan with reasonable certainty as to claim scope.

All of the claims in the Patents-in-Suit have a pharmacokinetic limitation because they all require that a certain "blood plasma concentration" be either "attained" or "achieved" ***for*** a particular amount of time. Exs. A-D at claim 1; *see also* Declaration of Dr. Michael Mayersohn ("Mayersohn Decl.") ¶ 55; *In re Cyclobenzaprine HCl Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1067 (Fed. Cir. 2012) ("Pharmacokinetics is the study of what a person's body does to a drug after administration."). But neither "attained" or "achieved" is a term of art in pharmacokinetics. Mayersohn Decl. ¶ 56. Thus, a person of skill in the art would typically understand the terms as per their common usage, which generally pertains to something happening at a single point in time, rather than a period of time. *Id.* ¶ 61. However, the preposition "for"—which is also present in the claims—can indicate something occurring over a period of time. Thus, the Patents-in-Suit could mean multiple things to a skilled artisan

[14] *See* note 11.

because the claims contain indicators of *both* a specific point in time *and* of something occurring over a period of time. *Id.* ¶ 62. In other words, because the terms do not agree grammatically, they would not be readily understood by a person of ordinary skill in the art to have one particular meaning. *Id.*

Complicating matters further is the fact that there is no technical discussion of pharmacokinetics in the specification—indeed, common pharmacokinetic terms such as "T_{max}," "C_{max}," "C_{min}," "PK profile," and "AUC" (area under the curve) are not found in the Patents-in-Suit anywhere**.** *Id.* ¶ 48. Moreover, there is only one figure even related to pharmacokinetics, and that figure concerns *in vivo* data from rabbits, not humans. *Id.* ¶¶ 52, 53, 54; Ex. A, '122 pat., Fig. 1. Furthermore, neither the claims nor the specification states the time the blood plasma concentration should be measured, or whether the measurement must be made at "steady state." Mayersohn Decl. ¶ 57; *see also Pfizer Inc. v. Teva Pharm. USA, Inc.*, 855 F. Supp. 2d 286, 293-94 (D.N.J. 2012) (construing claims; finding no steady state requirement); *Allergan, Inc. v. Watson Labs., Inc.-Fla.*, 869 F. Supp. 2d 456, 508-509 (D. Del. 2012) (finding claims required "one or more steady-state pharmacokinetic parameters"; "steady state blood levels"; "steady state C_{max} and C_{min}"; and "steady state AUCs"). Fundamentally, while the claims call for measurement of the blood plasma concentration, the person of ordinary skill in the art would not be able to discern how (out of multiple possible ways) to take that measurement, thereby rendering the term indefinite.

In sum, the claims and specification of the Patents-in-Suit are dissimilar to how pharmacokinetic concepts are usually claimed and described. Mayersohn Decl. ¶ 58; *see also In re Cyclobenzaprine*, 676 F.3d at 1067 (claim required a "maximum blood plasma concentration (C_{max}) within the range of about 80% to 125% of about 20 ng/mL of cyclobenzaprine HC1 and

an AUCo–168 within the range of about 80% to 125% of about 740 ng hr/mL and a T_{max} within the range of 80% to 125% of about 7 hours following oral administration...."); *Purdue Pharma L.P. v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1366 (Fed. Cir. 2001) ("Despite Roxane's arguments to the contrary, the T_{max}, C_{max}, T_{min}, and C_{min} values of the invention can be read in a graph entitled 'Bioavailability of CR Oxycodone'."); *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1322-23 (Fed. Cir. 2000) (claims directed to a method of treating pain by administering a sustained-release dosage . . . wherein the maximum plasma concentration (C_{max}) achieved was more than twice the plasma level of the opioid at approximately 24 hours after administration (C_{24})); *Abbott Labs. v. Andrx Pharm., Inc.*, 452 F.3d 1331, 1339 (Fed. Cir. 2006) ("[W]e agree with the district court's elaboration on the pharmacokinetic parameters of claim 4 . . . [1] maximum peak concentrations of the erythromycin derivative are lower than those produced by an immediate release pharmaceutical composition, [2] area under the concentration-time curve are substantially equivalent to that of the immediate release pharmaceutical composition and, [3] the minimum plasma concentration are substantially equivalent to that of the immediate release pharmaceutical composition.").

Thus, because: (i) "achieved" and "attained" are not terms of art; (ii) the claims are gramatically inconsistent; and (iii) there is no guidance given in the specification, Defendants' construction properly captures many possible meanings a skilled artisan could ascribe to the terms "achieved" and "attained" when attempting to determine the scope of the claim.

2. Plaintiffs pluck "and maintained" out of thin air.

In contrast to Defendants' well-reasoned construction—and despite the dearth of disclosure regarding the pharmacokinetics of the claimed invention—Plaintiffs take the position that "achieve" actually means, "achieve ***and*** maintain." The word "maintain," however, is not in

either the claims or the specification of the Patents-in-Suit, and indeed, is plucked out of thin air.[15]

Plaintiffs' citations in the March 23, 2015 Joint Claim Construction Statement (D.I. 58)) indicate that Plaintiffs are relying on references to the claimed formulation being a "sustained" release formulation. But as the Federal Circuit has explained, construing a claim based on terms not appearing in the claims (*e.g.*, "maintain") is quite dangerous:

> The danger of improperly importing a limitation is even greater when the purported limitation is based upon a term not appearing in the claim. "If we once begin to include elements not mentioned in the claim in order to limit such claim . . . , we should never know where to stop."

Amgen, 314 F.3d at 1325 (quoting *Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 990 (Fed. Cir. 1999)); *see also Source Vagabond*, 753 F.3d at 1299-300 (approving the district court's statement that: "an 'analysis' that adds words to the claim language [without support in the intrinsic evidence] . . . does not follow 'standard canons of claim construction.'").

3. "And maintain" is ambiguous.

Moreover, even if "and maintain" was supported by the intrinsic record—which it is not—Plaintiffs' construction still fails due to ambiguity. The purpose of claim construction is to "determin[e] the meaning and scope of the patent claims asserted to be infringed." *Markman v. Westview Instruments*, 52 F.3d 967, 976 (Fed. Cir. 1995), *aff'd*, 116 S. Ct. 1384 (1996). The additional phrase "and maintain" does not provide clarity to the claim terms for several reasons.

For example, the claimed plasma concentrations could refer to multiple possible pharmacokinetic parameters, such as C_{min} or C_{avg}. Mayersohn Decl. ¶ 65.

[15] And there is certainly no evidence that a word ("achieve") should be construed as having additional properties—*i.e.*, how can "achieve" mean "achieve ***and*** maintain?" This distorts the plain and ordinary meaning. The same analysis applies to "attained." *See* Mayersohn Decl. ¶ 61 ("achieve" and "attain" refer to single points in time).

Furthermore, in pharmacokinetics, "maintenance" of a blood plasma concentration ***requires*** a defined range between which a concentration must be observed. Mayersohn Decl. ¶ 69. More specifically, "maintenance" requires a reference value that can be measured against a C_{min} and C_{max}, neither of which is provided by the Patents-in-Suit. *Id.* Thus, because there is no C_{max} - C_{min} range provided by the Patents-in-Suit, the precise meaning of the pharmacokinetic terms is not elucidated by Plaintiffs' addition of the word "maintain." *Id.* ¶¶ 68-69.

For all of these reasons, Defendants respectfully request that the Court recognize the multiple meanings associated with the "achieved/attained" terms, as Defendants provide.

E. "Ethanol"

Term	Defendants' Construction	Plaintiffs' Construction
"ethanol"	Multiple concepts can exist with ethanol's plain and ordinary meaning(s), including but not limited to: • Pure ethanol; • ethanol containing "some water"; • ethanol containing "some other solvents"; • ethanol containing "some water" and "some other solvents"; • not less than 92.3 percent and not more than 93.8 percent, by weight, corresponding to not less than 94.9 percent and not more than 96.0 percent, by volume, at 15.56°, of C_2H_5OH; • not less than 99.2 percent, by weight, corresponding to not less than 99.5 percent, by volume, at 15.56°, of C_2H_5OH; • not less than 95.1 per cent v/v (92.6 per cent w/w) and not more than 96.9 per cent v/v (95.2 per cent w/w) of C_2H_6O (Mw 46.07) at 20°C, and water; • not less than 99.4% v/v or 99.0% w/w and not more than 100.0% v/v or 100.0% w/w of C_2H_5OH; • not less than 95.1 vol% and not more than 95.6 vol% (by specific gravity) of C_2H_6O at 15° C. The above list is not meant to be comprehensive. (*See* n.11).	"pharmaceutically-acceptable ethanol of a quality such that it will meet pharmacopoeial standards (such as are described in the US, British, European and Japanese pharmacopoeias) and as such will contain some water and possibly other organic solvents, for example ethanol in the US Pharmacopeia contains not less than 94.9% by volume and not more than 96.0% by volume of ethanol when measured at 15.56° C, and dehydrated alcohol in the US Pharmacopeia contains not less than 99.5% ethanol by volume when measured at 15.56° C."

Defendants' construction for the term "ethanol" is similar to Plaintiffs' in that both acknowledge: (i) skilled artisans understand that there is no single plain and ordinary meaning for "ethanol"; (ii) various forms and grades of ethanol can be used in pharmaceutical preparations; and (iii) the claims do not require one specific form or grade of ethanol to be used. As a result, regardless of which construction the court chooses, the claims are indefinite due to, *inter alia*, the multiple grades of ethanol available to the skilled artisan.[16]

Plaintiffs' construction is faulty, however, because Plaintiffs improperly treat certain language in the specification as an express definition. Defendants' construction holds true to the *guidance* given in the specification, but also provides specific examples of the different understandings of ethanol—and the different options available to a skilled artisan—which the prosecution history makes clear is required. The importance of the exact grade of ethanol has also been recognized by the courts. *See In re Armodafinil Patent Litig.,* 939 F. Supp. 2d 456, 480-81 (D. Del. 2013) ("[A]s the plaintiffs correctly point out, 'ethanol' can be interpreted more broadly than just absolute ethanol and, in fact, [the patent] describes more than one type of ethanol, including absolute ethanol, azeotropic ethanol, and denatured ethanol"; "the proper interpretation of ethanol depends upon the totality of the circumstances"). Accordingly, Defendants' construction for the term "ethanol" should be adopted, and Plaintiffs' construction should be rejected.

1. The specification only provides guidance, not a definition.

[16] This is because, depending on how and when ethanol contents are measured, there may be variances in the composition; presence/absence of varying amounts of water; azeotropic or similar bonding within ingredients; presence/absence of other ingredients that may "comprise" the formulation; etc. *See also In re Armodafinil Patent Litig.*, 939 F. Supp. 2d 456, 480-81 (D. Del. 2013).

There is guidance in the specification as to the term "ethanol"[17] (which Plaintiffs adopt for their construction), but the patentees did not act as their own lexicographer, and neither the specification nor claim includes a specific ethanol source or definition. Accordingly, the court must discern what constitutes ethanol's plain and ordinary meaning(s). *Hill-Rom Servs.*, 755 F.3d at 1371 (proper to "depart from the plain and ordinary meaning of claim terms based on the specification in only two instances: lexicography and disavowal.").

The specification states:

> It will be understood by the skilled person that the pharmaceutically-acceptable alcohol will be of a quality such that it ***will meet pharmacopoeial standards (such as are described in the US, British, European and Japanese pharmacopoeias)*** and as such will contain ***some water and possibly other organic solvents***, for example ethanol in the US Pharmacopeia contains ***not less than 94.9% by volume and not more than 96.0% by volume*** of ethanol when measured at 15.56° C. ***Dehydrated alcohol in the US Pharmacopeia contains not less than 99.5% ethanol*** by volume when measured at 15.56° C.

Ex. A, '122 pat., col. 7, ll. 32-42 (emphasis added).

The above text only sets forth the minimum standards for "pharmaceutically-acceptable" ethanol. If anything, the specification prompts the question: "what exactly are these *minimal* standards to which the specification refers?" It does not provide a single, limited definition for ethanol. Thus, although the passage cited above is *instructive*, it does not provide a definition with clear boundaries and scope—and thus, it is not proper to use it as a construction for the term "ethanol," as Plaintiffs suggest. *See Hill-Rom Servs.*, 755 F.3d at 1373 (finding no lexicography). Plaintiffs' proposed construction should be rejected.

2. Defendants' construction adheres to the specification.

In contrast, Defendants' construction follows the guidance provided in the specification

[17] There is nothing in the claims themselves.

and ***also*** reflects what the various pharmacopoeias referenced above specifically say. Thus, Defendants' construction incorporates all appropriate ethanol definitions.

First, as to the specification's reference to "pharmacopoeial standards (such as are described in the US, British, European and Japanese pharmacopoeias)," Defendants' construction is supported as follows:

Defendants' Construction	Support
not less than 92.3 percent and not more than 93.8 percent, by weight, corresponding to not less than 94.9 percent and not more than 96.0 percent, by volume, at 15.56°, of C_2H_5OH	*Alcohol*, *in* ***United States Pharmacopeia*** *23, National Formulary 18* (1995) ("Alcohol contains not less than 92.3 percent and not more than 93.8 percent, by weight, corresponding to not less than 94.9 percent and not more than 96.0 percent, by volume, at 15.56°, of C_2H_5OH.") (Ex. P).
not less than 95.1 vol% and not more than 95.6 vol% (by specific gravity) of C_2H_6O at 15° C	*Ethanol*, *in The* ***Japanese Pharmacopoeia****: JP XIII* (13th ed. 1996) ("Ethanol contains not less than 95.1 vol% and not more than 95.6 vol% (by specific gravity) of C_2H_6O at 15° C.") (Ex. Q).
not less than 95.1 per cent *V/V* (92.6 per cent *m/m*) and not more than 96.9 per cent *V/V* (95.2 per cent *m/m*) of C_2H_6O (*Mw* 46.07) at 20°C, and water	- *Ethanol (96 per cent)*, ***in European Pharmacopoeia*** (3d ed. Supp. 1999) ("Ethanol (96 per cent) contains not less than 95.1 per cent *V/V* (92.6 per cent *m/m*) and not more than 96.9 per cent *V/V* (95.2 per cent *m/m*) of C_2H_6O (M_r 46.07) at 20 °C, and water.") (Ex. R). - *Ethanol (96 per cent)*, *in* 1 ***British Pharmacopoeia*** (1999) ("Ethanol (96 per cent) contains not less than 95.1 per cent *V/V* (92.6 per cent *m/m*) and not more than 96.9 per cent *V/V* (95.2 per cent *m/m*) of C_2H_6O (M_r 46.07) at 20°C, and water.") (Ex. S).

See Declaration of Dr. Philip Gould ("Gould Decl.") ¶ 29.

Second, the specification's statement that "dehydrated alcohol in the US Pharmacopeia contains not less than 99.5% ethanol," is reflected in Defendants' construction as follows:

Defendants' Construction	Support
not less than 99.2 percent, by weight, corresponding to not less than 99.5 percent, by volume, at 15.56°, of C_2H_5OH	***Dehydrated Alcohol***, *in* ***United States Pharmacopeia*** *23, National Formulary 18* (1995) ("Dehydrated Alcohol contains not less than 99.2 percent, by weight, corresponding to not less than 99.5 percent, by volume, at 15.56°, of C_2H_5OH.") (Ex. P).
not less than 99.4% v/v or 99.0% w/w and not more than 100.0%	*Ethanol (Absolute Alcohol;* ***Dehydrated Alcohol****)*, *in* 1 ***British Pharmacopoeia*** (1993) ("Ethanol contains not less

v/v or 100.0% w/w of C_2H_5OH	than 99.4% v/v or 99.0% w/w and not more than 100.0% v/v or 100.0% w/w of C_2H_6O.") (Ex. T).

See Gould Decl. ¶ 30.

Lastly, Defendants' construction also accounts for the specification's statement that ethanol can contain "some water and possibly other organic solvents" because it includes pure ethanol; ethanol containing "some water"; ethanol containing "some other solvents"; and ethanol containing "some water" and "some other solvents." *See* Gould Decl. ¶ 31.

Thus, Defendants' construction is completely supported and should be adopted.

3. Plaintiffs cannot argue that specificity is not necessary.

The need for the specificity given by Defendants' construction is shown by, inter alia, the prosecution of the '680 patent, where the patentees overcame a prior art reference ("McLeskey") that disclosed the ***exact*** numerical percentages of ***every*** excipient by making distinctions between weight:volume and weight:weight ratios, based in part on the exact type of ethanol used. Ex.I, '680 pat. PH, 1/17/2012 Sawchuk § 132 Decl. at 9, n. 1 ("*McLeskey* does not indicate whether the ethanol used in its castor oil fulvestrant composition is dehydrated ethanol or the binary azeotropic ethanol composition containing about 96% ethanol by volume.").

Thus, Plaintiffs now cannot be heard say that it is not necessary to specify the scope of the <u>*exact*</u> grades and/or forms of ethanol that the claims encompass. *See Infection Prevention Techs., LLC v. Lumalier Corp.*, No. 10-12371, 2012 WL 3248232, at *9 (E.D. Mich. Aug. 8, 2012) (claims required a characteristic that the patentee argued during prosecution was "critical" over the prior art). The need for the specificity reflected in Defendants' construction is further supported by the Declaration of Dr. Philip Gould, which explains that there are multiple forms of alcohol used in pharmaceutical preparations and thus, the term "pharmaceutically-acceptable ethanol"—which is used in the specification and Plaintiffs' construction—necessarily has

multiple meanings. Gould Decl. ¶¶ 20-23; *see also Markman*, 116 S. Ct. at 1394 ("[W]here the qualities of substances . . . necessary to the comprehension of the language of the patent are unknown to the judge, the testimony of witnesses may be received upon these subjects.").

For all of these reasons, Defendants respectfully request that the Court adopt their proposed construction for the term "ethanol."

F. "Hormonal dependent benign or malignant disease of the breast or reproductive tract"

Term	Defendants' Construction	Plaintiffs' Construction
"hormonal dependent benign or malignant disease of the breast or reproductive tract"	Various words or phrases within the claim term have a plain and ordinary meaning. However, the arrangement of the words within this claim term renders the term "benign or malignant disease" to be redundant. To the extent that this term is not redundant, the claim term is indefinite. Moreover, "hormonal dependent" is a term of degree. The Federal Circuit has held that for terms of degree, they must be defined or clarified in the specification or claim to identify more than merely *some* standard for measuring the scope of the term of degree phrase, and that a failure to do so renders the term indefinite. *See Interval Licensing LLC v. AOL, Inc.*, 766 F.3d 1364, 1370-71 (Fed. Cir. 2014). Here, the specification and claim renders no guidance as to the scope of hormonal dependency required, instead, it depends on the unpredictable vagaries of any one person's opinion; therefore, the claim term is indefinite. *Id.* at 1371.	Plain and ordinary meaning to a person of skill in the art.

Defendants do not offer their own construction for the term "hormonal dependent benign or malignant disease of the breast or reproductive tract," but request that this Court fully reserve the issue and Defendants' right to move for summary judgment or raise at trial that the phrase renders the claims invalid under § 112 for indefiniteness for at least two reasons.

First, it is clear that ***all*** diseases of the "breast or reproductive tract" are either "benign" or "malignant," *i.e.*, a disease cannot be neither benign nor malignant. Thus, under the plain and ordinary meaning of the term, the phrase "benign or malignant" does not limit the scope of the

claim, and is redundant. *Jack Guttman, Inc. v. Kopykake Enters. Inc.*, 302 F.3d 1352, 1357 (Fed. Cir. 2002) (holding that dictionary definition of "tortuous"— "marked by repeated twists, bends, or turns"—would make the phrase "tortuous bend" redundant). If Plaintiffs argue that the term is ***not*** redundant, then it is indefinite.[18]

Second, "hormonal dependent" is a term of degree. While such claims are not "inherently indefinite," "it is not enough . . . to identify '*some standard* for measuring the scope of the phrase.'" *Interval Licensing LLC v. AOL, Inc.*, 766 F.3d 1364, 1370-71 (Fed. Cir. 2014). Indeed, a patent does not satisfy the definiteness requirement of § 112 because "a court can ascribe *some* meaning to a patent's claims.'" *Id.* at 1371. Rather, the "claims, when read in light of the specification and the prosecution history, ***must*** provide objective boundaries for those of skill in the art." *Id.* (emphasis added) (citing *Nautilus*, 134 S. Ct. at 2130). A failure to provide such clear boundaries renders the term indefinite. *Id.* Here, the specification and claims render no guidance as to the scope of hormonal dependency required, instead, it depends on the unpredictable vagaries of any one person's opinion. Thus, the term is indefinite. *See id.* Defendants submit that these issues should be presented for the Court's decision on a fully-developed record.

G. "Formulation"

The term "formulation" is present in every independent claim of the '680 and '139 Patents (and is thus also present in every dependent claim of these two patents).

Term	Defendants' Construction	Plaintiffs' Construction
"formulation"	Plain and ordinary meaning.	Plain and ordinary meaning to a person of skill in the art, i.e., pharmaceutical formulation.

[18] To date, Plaintiffs have not informed Defendants of their position on this issue.

While the parties agree the term "formulation" should be given its plain and ordinary meaning, Plaintiffs' proposal adds the additional limitation that it be a ***pharmaceutical*** formulation. While the term "formulation" is used in the claims of the '680 and '139 patents, the term "pharmaceutical formulation" is used in the claims of the '122 and '160 patents. Under the principle of claim differentiation, "[t]here is presumed to be a difference in meaning and scope when different words or phrases are used in separate claims." *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998). Plaintiffs improperly seek to narrow the meaning of "formulation" as it appears in the claims of the '680 and '139 patents by injecting the term "pharmaceutical." That term, however, is absent from the claims of the '122 and '160 patents. *Compare* Ex. C, '680 pat., claims 1 & 9, and Ex. D, '139 pat., claims 1 & 11 *with* Ex. A, '122 pat., claims 1 & 5, and Ex. B. '160 pat., claims 1 & 2.

Accordingly, the term "formulation" as it appears in the '680 and '139 patent claims should be given its plain and ordinary meaning as proposed by Defendants, which is not limited by the term "pharmaceutical." Plaintiffs' attempt to inject a limitation should not be permitted.

Defendants' construction is also supported by the specification, which uses the term "formulation" generally, without reference to any particular clinical or medical use. *See, e.g.*, Ex. A, '122 pat., col. 1, ll. 8-15. In contrast, the specification uses the phrase "pharmaceutical formulation" when referring to a formulation adapted for medical or clinical use. *See, e.g.*, *id.*, col. 11, ll. 1-3, 18-22 ("A further feature of the invention is a pharmaceutical formulation adapted for intra-muscular injection, as defined above, for use in medical therapy [and] for the treatment of a benign or malignant disease . . . .").

V. Conclusion.

For all of these reasons, Defendants respectfully request that the Court adopt all of their proffered constructions.

Dated: May 7, 2015

Respectfully submitted,

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